UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE LUMIFY	Civil Action No. 21-16766 (RK) (RLS) (CONSOLIDATED) *Document Electronically Filed*

PLAINTIFFS' OPENING *MARKMAN* BRIEF

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Pursuant to Local Patent Rule 4.5(a), Plaintiffs Bausch & Lomb, Inc., Bausch & Lomb Ireland Limited and Eye Therapies, LLC (collectively, "Plaintiffs") respectfully submit this opening *Markman* brief concerning U.S. Patent No. 11,596,600 ("the '600 patent"), Ex.[1] 1.

I. INTRODUCTION

This case involves infringement of the '600 patent based on submission by Defendants Dr. Reddy's Laboratories Inc., Dr. Reddy's Laboratories, S.A., Slayback Pharma LLC and Slayback Pharma India LLP (collectively, "Defendants") of an Abbreviated New Drug Application ("ANDA") requesting FDA approval to market generic copies of Lumify redness reliever eye drops. *See, e.g.*, Ex. 11 (Eyewire 2022) at 1; 35 U.S.C. § 271(e)(2)(A). Through their ANDA, Defendants seek to capitalize on the success of Lumify, which is approved for relieving redness of the eye due to minor eye irritations, contains 0.025% wt./vol as its sole active ingredient, and its use is covered by the claims of the '600 patent. *See, e.g.*, Ex. 12 (Lumify Label) at 2. Lumify received FDA approval in December 2017, and immediately garnered acclaim in the medical community as "#1 eye doctor recommended" redness reliever eye drop. Ex. 13 (Lumify Brochure) at 1. Utilizing the inventive methods of the '600 patent, Lumify achieves a reduction in eye redness with virtually no rebound redness and tachyphylaxis—two side effects that had plagued the decades-long industry-leading commercial eyedrops, like the VISINE products, All Clear, and Ocu-Clear. Decl. of Dr. William B. Trattler in Support of Plaintiffs' Opening *Markman* Brief ("Trattler Decl.") ¶ 30.

Defendants have proposed two phrases from the claims of the '600 patent for construction: 1) "human in need of said reduction of eye redness," and 2) "as the sole active ingredient."

[1] "Ex. __" refers to the exhibits to the Declaration of Bryan C. Diner in Support of Plaintiffs' Opening *Markman* brief.

Plaintiffs believe these phrases should be construed according to their plain and ordinary meaning based on how a person of ordinary skill in the art ("POSA") would understand them in light of the relevant intrinsic and extrinsic evidence. Defendants, on the contrary, have proposed constructions that are at odds with the plain language of the claims themselves, the patent specification, and the prosecution history.

Plaintiffs submit that a person of ordinary skill in the art reading the phrase "human in need of said reduction of eye redness" in context of the claimed method of which it is part and consistent with specification and prosecution history would have understood it to mean "a human having ocular hyperemia, where such hyperemia is reduced by vasoconstriction. The second clause is critical because it captures the essence of the inventive methods as emphasized throughout the intrinsic record—namely, *achieving* a reduction in eye redness." Defendants, on the other hand, propose that the phrase should be construed as "having ocular hyperemia." Defendants' proposal simply repeats language from the preamble of the claim, treating this phrase as though it adds nothing beyond what is already present elsewhere. Far from faithfully attempting to ascertain the true meaning of the disputed phrase, Defendants instead seek to improperly whitewash critical language from the claimed administration step of which the phrase is part.

Plaintiffs further submit that a person of ordinary skill in the art reading the phrase "as the sole active ingredient" in the '600 patent method and in view of the specification and prosecution history would have understood it to mean "[administering brimonidine] as the only active ingredient to affirmatively reduce redness in a person having ocular hyperemia." The prosecution history particularly evidences how the Patentee understood that phrase, having unequivocally surrendered and disclaimed the administration of brimonidine as part of a dosing protocol with any other active ingredient to distinguish the claimed redness reducing methods from cited prior

art and induce the patent grant. Defendants propose that the phrase should be construed as "without any other active ingredient in the ocular drop." That proposal, however, opens the method up to administering additional drops that contain other active ingredients, running directly contrary with the claim language as a whole as well as clear and unequivocal statements made by the Patentee during prosecution in order to secure allowance of the '600 patent.

In each instance, Defendants' proposed constructions for the disputed phrases ignore and significantly depart from how those phrases would have been understood by a person of ordinary skill in in light of the intrinsic record. This is nothing more than a litigation-driven tactic designed to chip away at Defendants' heavy burden of proving invalidity and revive references and positions that the Patent Examiner duly considered during prosecution before allowing the claims to issue. It should be rejected as such.

For these reasons and as discussed further below, Plaintiffs respectfully request that the Court adopt Plaintiffs' proposed constructions and reject Defendants' constructions.

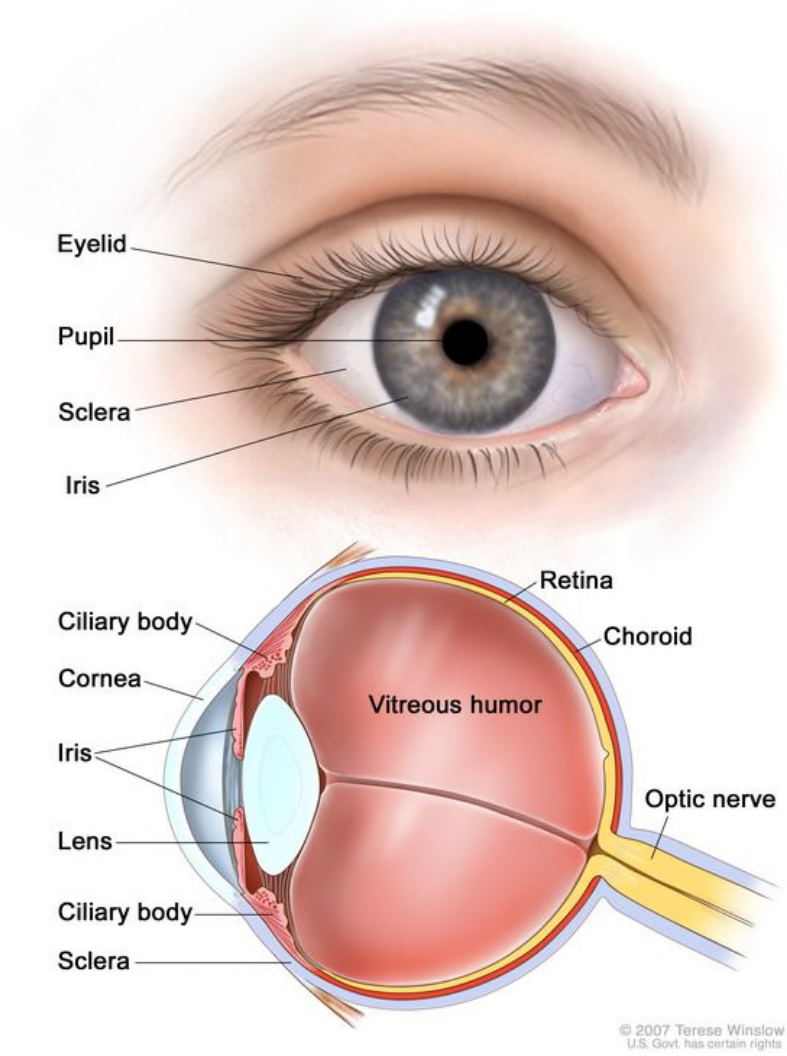
II. TECHNOLOGICAL BACKGROUND

To provide background concerning the technology of the '600 patent, and consistent with how a person of ordinary skill in the art would interpret the disputed claim phrases, Plaintiffs have submitted a declaration from William B. Trattler, M.D. From a time prior to August 1, 2008—the earliest effective filing date of the '600 patent—Dr. Trattler has been a practicing ophthalmologist specializing in refractive, corneal and cataract eye surgery. Trattler Decl. ¶ 2. Dr. Trattler routinely sees patients with eye redness (ocular hyperemia) caused from various conditions and treatments. *Id.* at ¶ 12. He is familiar with the well-known commercial redness relievers like VISINE and others that existed before the earliest filing date of the '600 patent and before the development of Lumify. *Id.* He has worked with Lumify clinically and has recommended it to his patients

presenting with eye redness. He would have been considered at least a person of ordinary skill in the art to which the invention of the '600 patent pertains, under both Plaintiffs' and Defendants' definitions, and is qualified to express his opinions in this matter. *Id*. ¶¶ 21-24.

A. The Field to Which the '600 Patent Pertains

The field to which the invention of the '600 patent pertains involves ophthalmic products topically administered to reduce eye redness or ocular hyperemia. '600 patent, 4:40-5:6, 5:51-61, 7:24-33, 14:21-29. Such ophthalmic products target parts of the eye known as conjunctiva, the episclera, and the sclera, which can be seen in the illustration below. *Id*. at 1:23, 14:21-23, 30-36; Trattler Decl. ¶ 25.



In this illustration, the sclera is the visible "white" of the eye. Trattler Decl. ¶ 26. The conjunctiva is a clear, thin tissue that covers the sclera. *Id*. The sclera consists of several layers, including the episclera, which is a thin tissue resting on the outer surface of the eyeball. *Id*. The conjunctiva, episclera, and sclera all have blood vessels, which, when dilated, present as eye redness. *Id*.

Eye redness or hyperemia refers to an ocular condition caused by vasodilation—an increase in the diameter of the blood vessels due to the influx of blood. Ex. 1 ('600 patent) at 1:20-25. The dilated blood vessels become congested and engorged with blood, making the eyes appear red or hyperemic. *Id*. at 4:49-51. Conversely, constricting dilated ocular blood vessels will decongest them, which on the surface can reduce redness and make the eyes appear whiter but can also cause an ischemic condition. *Id*. at 4:55-61. This is known as vasoconstriction. Trattler Decl. ¶ 27.

B. Commercial Prior Art Redness Relievers

All FDA-approved redness relievers before the filing of the '600 patent—including the VISINE products (tetrahydrozoline), All Clear (naphazoline), and Ocu-Clear (oxymetazoline)—were associated with adverse side effects, including rebound hyperemia and tachyphylaxis. Ex. 1 ('600 patent) at 16:2-7; Trattler Decl. ¶ 31. Rebound hyperemia occurs, for example, after the vasoconstrictive effects of the redness reliever wear off and compensatory vasodilation occurs to flood/engorge the vessels with blood to bring in the needed oxygen. Trattler Decl. ¶ 31. Eyes with rebound hyperemia thus present with more redness than before instillation of the redness reliever. Ex. 1 ('600 patent), 4:46-51; Trattler Decl. ¶ 31. Tachyphylaxis is a medical condition that manifests as a rapid decrease in drug effectiveness after repeated uses over time. Trattler Decl. ¶ 31. It could prompt consumers to instill more drops more frequently to obtain the same level of whitening, unwittingly leading to misuse and overuse of the drug. *Id*. The continued overuse of

the drug could lead to ocular toxicity as well as chronic swelling and redness (medicamentosa) even after discontinuation. Ex. 1 ('600 patent), 4:52-54; Trattler Decl. ¶ 31.

Eye care professionals often did not recommend these commercial redness relievers because of these side-effects. Trattler Decl. ¶ 30. They knew their patients used these over-the-counter ("OTC") products, and they accepted them as standard of care, for no better alternative existed. *Id.*

C. Previously Approved Uses of Brimonidine

Brimonidine tartrate, the active ingredient in Lumify, was previously used in much higher concentrations in various FDA-approved Alphagan products for treating glaucoma and reducing intraocular pressure (IOP): Alphagan (0.5% and 0.2% brimonidine) and Alphagan P (0.15% and 0.1% brimonidine). Trattler Decl. ¶ 33. At these high concentrations, use of the Alphagan products resulted in a high rate of hyperemia and allergic ocular reactions in patients. *Id*. Ocular hyperemia was repeatedly identified as one of the most common side effects of the drug in glaucoma patients. *Id*. Although at high concentrations brimonidine (0.5% and 0.2%) could vasoconstrict, that effect was no longer reported on the label for Alphagan P (0.15% and 0.1% brimonidine).

D. Lumify's Excellent Redness Reducing Ability Without Rebound Hyperemia and Tachyphylaxis Has Made It a Commercial Success

Lumify demonstrated excellent redness reducing efficacy in clinical trials, working within one minute and reducing redness for up to eight hours. *See, e.g.*, Ex. 12 (Lumify Label) at 2. Based on its review of clinical study results, the U.S. Food and Drug Administration ("FDA") stated that Lumify did not show tachyphylaxis or rebound hyperemia and predicted that it would provide a potential advantage to consumers of an OTC product, which typically lack doctor supervision and can be susceptible to consumer overuse and misuse. Ex. 14 (Lumify NDA Summary) at 2. In just three months after Lumify's launch at the end of 2017, the FDA's prediction came to fruition.

Lumify became the #1 eye doctor recommended redness relieving drop, drawing praise from doctors for its advantageous efficacy and safety profile. Ex. 13 (Lumify Brochure) at 1. It simultaneously disrupted and revitalized a stagnant redness reliever market, while garnering significant commercial success.

III. THE DISCLOSURE AND CLAIMS OF THE PATENTS-IN-SUIT

A. Asserted Claims from the ’600 Patent

The ’600 patent claims are generally directed to a method for reducing eye redness in a human subject having ocular hyperemia (eye redness), comprising topically administering 0.025% brimonidine as the sole active ingredient at a pH between 5.5 and 6.5. Plaintiffs currently assert claims 12 and 28 of the ’600 patent, which both depend from claim 1.

Claim 12 further limits claim 1 by reciting that “the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye.” Written in independent form, claim 12 reads as follows:

> 12. A method for reducing eye redness in a human subject having ocular hyperemia, comprising topically administering to an eye of said human in need of said reduction of eye redness an ocular drop comprising about 0.025% weight by volume brimonidine as the sole active ingredient, wherein the ocular drop has a pH between 5.5 to 6.5, and wherein the eye redness of said human is not associated with an ocular disease or the result of a surgical procedure on the eye.

Ex. 1 (’600 patent) at 22:34-49, 23:1-3.

Claim 28 further limits claim 1 by reciting that the amount of brimonidine administered in the method of claim 1 is 0.025%, and when written in independent form reads as follows:

> 28. A method for reducing eye redness in a human subject having ocular hyperemia, comprising topically administering to an eye of said human in need of said reduction of eye redness an ocular drop comprising 0.025% weight by volume brimonidine as the sole active ingredient, wherein the ocular drop has a pH between 5.5 to 6.5.

Ex. 1 (’600 patent) at 22:34-39, 24:22-23.

B. The Specification of the ’600 Patent

The ’600 patent describes administering low-concentration brimonidine to achieve more effective vasoconstriction and reduce eye redness with significantly less rebound hyperemia compared to prior art redness relievers. Ex. 1 (’600 patent), 2:43-55; 4:40-54, 4:62-5:6. The first substantive paragraph of the specification identifies eye redness with conjunctival hyperemia. *Id*. at 1:23 (referring to “eye redness (conjunctival hyperemia)”). A POSA would appreciate that reducing eye redness in the conjunctiva, sclera and episclera makes the eyes appear whiter. Trattler Decl. ¶ 36. The ’600 patent describes inventive methods of using brimonidine to achieve “a more effective scleral whitening (i.e., whiter shades of scleral color) than possible with prior art compositions and methods, as a result of more effective vasoconstriction….” Ex. 1 (’600 patent) at 14:30-36. It discloses, moreover, several clinical studies substantiating this claim. *E.g.*, Examples 1, 4, and 5 and the studies embodied in Figures 5A-C.

The low-concentration brimonidine used in the compositions of the methods for reducing redness can range from about 0.0001% to about 0.05%, Ex. 1 (’600 patent), 3:60-65, and the specification identifies various preferred amounts including about 0.025%. *See, e.g., id*. at 4:8-13, 5:65-67, 6:8-11, 7:19-23, 8:26-30, 11:47-52. The specification discloses multiple inventive embodiments, some of which dose brimonidine in combination with other active ingredients, *see, e.g., id*. at 9:53-55, 15:61 to 17:3, 16:57-58 and 65-66, and others that dose brimonidine as the sole active ingredient. *See id*. at 7: 34-40, 8:19-25, 9:46-49, 10:21-26, Examples 1, 4, and 5 and the studies embodied in Figures 5A-C.

Example 1 of the ’600 patent shows the results of treating the left eye of a patient having ocular hyperemia with various low-doses of brimonidine as the sole active ingredient in accordance with the invention. Ex. 1 (’600 patent), 20:36-67. In the patient’s right eye, in separate

experiments, 0.05% tetrahydrozoline, 0.025% oxymetazoline, and 0.033% naphazoline were instilled for comparison purposes. *Id*. The results are visibly shown in Figs. 4A-C, and Example 1 concludes these "results clearly demonstrate significant scleral whitening brightening effects of treatment with brimonidine as compared with treatment with prior art compositions." *Id*. at 20: 41-43.

Example 4 of the '600 patent is another clinical study that compared the eye redness reducing ability in fifteen patients between 0.018% brimonidine, administered as the sole active ingredient in one eye, and VISINE Original® (tetrahydrozoline) administered as the sole active ingredient in the other eye of each patient. Ex. 1 ('600 patent), 21:57-22:19. After a single application, 0.018% brimonidine exhibited a reduction in redness score of 68.71% compared to 31.06% for VISINE Original®. *Id*. at 22:1-6. Additionally, when brimonidine was administered at 0.05% to fifteen patients as the sole active ingredient, only one patient experienced rebound hyperemia (6.6%), whereas 26.6% of those patients experienced rebound hyperemia with VISINE Original®. *Id*. at 22:7-10.

Example 5 is a clinical study involving seven patients with chronic red eyes. Ex. 1 ('600 patent), 22:21-31. One of the patients was treated with 0.015% brimonidine alone, while the other eye received Naphcon-A® (0.025% naphazoline). *Id*. In a patient satisfaction assessment, all patients reported reduced redness with 0.015% brimonidine and 42% of them preferred brimonidine, whereas none preferred Naphcon-A®. *Id*. at 22:27-31.

C. The Prosecution History of the '600 Patent

The application that became the '600 patent was filed on January 22, 2022. It was allowed on November 4, 2022, and granted as the '600 patent on March 7, 2023. Between the filing of the application and its allowance, two substantive Office Actions were issued by the USPTO Patent Examiner to which the Patentee submitted two corresponding responses.

As filed, application claim 1 read as follows:

> 1. A method for reducing eye redness in a human subject resulting from an ocular condition, comprising topically administering to an eye of said human an ocular drop comprising about 0.025% weight by volume brimonidine as the sole active ingredient, wherein the ocular drop has a pH between 5.5 to 6.5.

Ex. 1 ('600 patent), 22:34-39.

The first Office Action issued on August 5, 2022. The Patent Examiner rejected all pending claims in the application, including claim 1, for indefiniteness under 35 U.S.C. § 112(b). Ex. 9 ('600 patent file history, August 5, 2022 Office Action at 4). The Patent Examiner issued two rejections of claim 1 for obviousness under 35 U.S.C. § 103 in view of several prior art documents, which included Ex. 15 (U.S. Patent Application No. 2001/0031754 to Gil et al. ("Gil")), Ex. 10 (U.S. Patent No. 6,242,442 to Dean et al. ("Dean")), and Ex. 16 (U.S. Patent Application No. 2004/0219219 to Graham et al ("Graham")). *Id*. at 9 and 16.

Regarding the indefiniteness rejection, the Patent Examiner alleged that "eye redness" resulting from "an ocular condition" was unclear. Ex. 9 ('600 patent file history, August 5, 2022 Office Action at 4). In the November 4, 2022, response, the Patentee amended claim 1 to delete "resulting from an ocular condition" and to more particularly describe the human subject as "having ocular hyperemia" and, relatedly, as being "in need of said reduction of eye redness." As amended, claim 1 read as follows (deletions in strikethrough and additions in underline):

> 1 (Amended). A method for reducing eye redness in a human subject <u>having ocular hyperemia</u> ~~resulting from an ocular condition~~, comprising topically administering to an eye of said human <u>in need of said reduction of eye redness</u> an ocular drop comprising about 0.025% weight by volume brimonidine as the sole active ingredient, wherein the ocular drop has a pH between 5.5 to 6.5.

Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 2).

The Patentee addressed this rejection and the claim amendments in the "Remarks" section of the November 2022 response. *Id*. at 7. The Patentee stated that "[c]laim 1 has been amended to recite that the human has ocular hyperemia, which is eye redness caused by dilation of intact blood vessels in the conjunctiva, episclera and sclera, where such redness can be reduced by vasoconstriction of those blood vessels. *Id*. It also emphasized that eye redness as used in the claim 1 of the application (i.e., ocular hyperemia) is different from eye redness resulting from subconjunctival hemorrhage. *Id*. The Patentee specifically stated "[o]cular hyperemia is different than eye redness caused by subconjunctival hemorrhage, which is typically the result of trauma that breaks the ocular blood vessels, resulting in blood pouring out and settling beneath the conjunctiva. (citation omitted.) Redness resulting from subconjunctival hemorrhage cannot be reduced by vasoconstriction of the broken blood vessels." *Id*. The amendment and related arguments obviated this rejection, as the Patent Examiner did not reassert it in the next Office Action.

In the first obviousness rejection, the Patent Examiner alleged that the method of claim 1, among other claims, was obvious in view of Gil and Dean. In the second obviousness rejection, the Patent Examiner asserted that the claim 1 method was obvious in view of Dean, Gil, and Graham. Ex. 9 ('600 patent file history, August 5, 2022 Office Action at 16). In response, the Patentee argued that the Patent Examiner's combination of Gil and Dean was fatally defective. Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 12-14). The arguments made to distinguish Dean are particularly relevant.

Specifically, the Patentee argued that "Dean is not directed to treating eye redness, nor does it suggest using brimonidine, let alone low-dose brimonidine as the sole active ingredient, to affirmatively reduce eye redness in a patient having ocular hyperemia. Rather, Dean is directed to

combinations of brinzolamide and brimonidine for treating a different condition, i.e., lowering intraocular pressure (IOP)." *Id*. at 12 (emphasis original). The Patentee further argued that Dean is "far from guiding the skilled artisan to about 0.025% as the sole active ingredient to affirmatively reduce redness in a person having ocular hyperemia" and that "[t]his preferred range would have led the skilled person, if anywhere, to concentrations much higher than the instantly claimed concentrations of about 0.025% as the sole active." *Id*. at 13.

The Patentee continued to distinguish Dean, further characterizing how it understood the claimed invention and, therefore, how a POSA would have similarly understood the invention: "At bottom, while Dean hypothesizes that lowering the dose of brimonidine could reduce the *incidence* of hyperemia, it does not teach or suggest that low dose brimonidine as the sole active can reduce redness," and "[t]he invention here demonstrates that low-dose brimonidine, used on a human subject having ocular hyperemia, affirmatively *reduces* eye redness; whereas Dean suggests that lowering the dose of brimonidine my *induce* less redness (as a side effect), but does not teach or suggest *reducing redness* in a subject *having* ocular hyperemia." *Id*. (emphasis in original).

In the second Office Action of December 1, 2022, the Patent Examiner withdrew the indefiniteness rejection and both obviousness rejections in view of the Patentee's amendments and arguments. Ex. 18 ('600 patent file history, December 1, 2022 Office Action at 2-3). The Patent Examiner maintained a previous rejection under obviousness-type double patenting, which the Patentee removed with a terminal disclaimer and the application was allowed. *Id*. at 4-6. The '600 patent subsequently issued on March 7, 2022.

IV. LEGAL STANDARDS

A. The Law of Claim Construction

The words of a patent claim "are generally given their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (*en banc*) (internal quotation marks

and citation omitted). Indeed, it is "unjust to the public, as well as an evasion of the law, to construe [a patent claim] in a manner different from the plain import of its terms." *Id*. (internal quotation marks and citation omitted). "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person or ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id*. at 1313; *see also ResQNet.com, Inc. v. Lansa, Inc.*, 346 F.3d 1374, 1378 (Fed. Cir. 2003) ("Indeed, normal rules of usage suggest a 'heavy presumption' that claim terms carry their accustomed meaning in the relevant community at the relevant time."). "Importantly, the person or ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313.

Patent "claims, of course, do not stand alone." *Phillips*, 415 F.3d at 1315. "Rather, they are part of a fully integrated written instrument, consisting principally of a specification that concludes with the claims." *Id*. (internal quotation marks and citation omitted). "For that reason, claims must be read in view of the specification, of which they are a part." *Id*. (internal quotation marks and citation omitted). The specification "is always highly relevant to the claim construction analysis." *Id*. (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Indeed, the Federal Circuit had held that the construction of a claim term must be "consistent with the specification." *See, e.g.*, *Vitronics*, 90 F.3d at 1583; *Nystrom v. TREX Co., Inc.*, 424 F.3d 1136, 1147 (Fed. Cir. 2005) (adopting the definition of the claim term that was "consistent with the specification" of the patent); *Texas Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1207 (Fed. Cir. 2002) ("This plain meaning is consistent with the specification of the '481 and '561 patents.").

The Federal Circuit has further explained that "the specification necessarily informs the proper construction of the claims" and that the construction "that most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Phillips*, 415 F.3d at 1316 (quoting *Renishaw PLC v. Marposs Soceita' per Azioni*, 158 F.3d 1243 (Fed. Cir. 1998). This is because "[f]or claim construction purposes, the description may act as a sort of dictionary, which explains the invention and may define terms used in the claims." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995); *see also Network Commerce, Inc. v. Microsoft Corp.*, 422 F.3d 1353, 1360 (Fed. Cir. 2005) (limiting the term "download component" to a component capable of performing certain functions, based on the consistent usage in the specification because the claims cannot transcend the invention that entitles the inventor to a patent). The Federal Circuit has described the specification as "the single best guide to the meaning of a disputed claim" and has said that the specification is "usually . . . dispositive." *Id.* The intrinsic evidence for patent claim interpretation includes the claim language, specification, and prosecution history. *Phillips*, 415 F.3d at 1317; *see also Vitronics*, 90 F.3d. at 1583 (If "an analysis of the intrinsic evidence alone will resolve any ambiguity in a disputed claim term[,] . . . it is improper to rely on extrinsic evidence.") Additionally, so long as it does not "contradict the meaning of claims discernible from thoughtful examination of the . . . the intrinsic evidence[,]" *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999), courts may rely on extrinsic evidence, which "consists of all evidence external to the patent and prosecution history," including, for example, expert testimony. *Phillips*, 415 F.3d at 1317 (internal quotation marks and citation omitted). Expert testimony, in particular, "can be useful to a court for a variety of purposes, such as to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of technical aspects of the patent is consistent with

that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318.

B. A Person of Ordinary Skill in the Art

Claims are to be construed as they would be understood by a person of ordinary skill in the field at the time of invention. *Phillips*, 415 F.3d at 1313. The relevant time for the '600 patent is August 1, 2008, the filing date of the earliest provisional application, U.S. Appl. Ser. No. 61/137,714. Ex. 1 ('600 patent), 1. A person of ordinary skill in the art at the time would have been a team of individuals with experience and various skills relating to eye care, including, *inter alia*, the medical and pharmaceutical formulation arts. Trattler Decl. ¶ 22. The POSA also would have had access to team members with experience in chemistry, in designing and evaluating ophthalmic formulations, and/or in administering ophthalmic formulations to treat ocular conditions obtained by some combination of education and work experience. *Id.*

V. ARGUMENT

A. The Court Should Adopt Plaintiffs' Proposed Construction of the Claim Phrase "[human] in need of said reduction of eye redness"[2]

Defendants dispute the meaning of the claim phrase "human in need of said reduction of eye redness" recited in claim 1, which is incorporated in claims 12 and 28 by their dependency from claim 1. The parties' respective proposed constructions for the phrase are shown below.

Plaintiffs' Construction	Defendants' Construction
"a human having ocular hyperemia, where such hyperemia is reduced by vasoconstriction."	"having ocular hyperemia"

[2] The terms in brackets are the terms that are not in the phrases that Defendants proposed for construction, but they provide important context for the disputed phrases.

Reading the phrase "human in need of said reduction of eye redness" in context of the claimed method of which it is part and consistent with specification and prosecution history, a POSA would have understood it to mean "a human having ocular hyperemia, where such hyperemia is reduced by vasoconstriction." Defendants, on the other hand, propose that the phrase should be construed as "having ocular hyperemia." Defendants' proposal—which simply repeats language from the preamble—adds nothing to this phrase and, in fact, improperly whitewashes the "*in need of*" language from the claimed phrase, which is a core part of a manipulative step in the claimed method. Defendants' proposed construction is also inconsistent with how a POSA would have understood the phrase in light of the specification and prosecution history.

1. Plaintiffs' Proposed Meaning of "human in need of said reduction of eye redness" is Properly Tethered to the Intrinsic Record

Properly reading the phrase "human in need of said reduction of eye redness" in context of the fully claimed method of reducing eye redness, as well as the specification and prosecution history, a POSA would have understood the phrase to mean to "a human having ocular hyperemia, where such hyperemia is reduced by vasoconstriction." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) (adopting a claim construction that aligned with the intrinsic evidence to resolve any ambiguity in a disputed claim term); *see also Phillips v. AWH Corp.*, 415 F.3d 1303 1317 (Fed. Cir. 2005) (*en banc*) (the construction "that most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.")

At the outset, a POSA would have understood "eye redness" recited in the disputed phrase as ocular hyperemia. Trattler Decl. ¶ 52. The claims, specification, and prosecution history all align to consistently equate eye redness with ocular hyperemia. The claim preamble makes that clear from the beginning ("… reducing *eye redness* in a *human subject having ocular hyperemia*…). Ex. 1 ('600 patent), 22:34-35 (emphasis added). The first substantive paragraph of

specification identifies eye redness with conjunctival hyperemia and identifies several conditions that will cause eyes to appear red or hyperemic. *Id*. at 1:23 (…"eye redness (conjunctival hyperemia)…"), 2:27-30; and Trattler Decl. ¶ 52. During prosecution, the Patentee similarly equated eye redness with ocular hyperemia to address the Examiner's indefiniteness position relating to the meaning of eye redness as recited in the claims: "Claim 1 has been amended to recite that the human has ocular hyperemia, which is eye redness…."[3]

A claimed term or phrase should be interpreted as part of the claim element to which it belongs. *See Phillips*, 415 F.3d at 1314 (citing *Vitronics*, 90 F.3d at 1582); *ACTV, Inc. v. Walt Disney Co.*, 346 F.3d 1082, 1088 (Fed. Cir. 2003) (finding that "[w]hile certain terms may be at the center of the claim construction debate, the context of the surrounding words of the claim also must be considered in determining the ordinary and customary meaning of those terms"). Proper claim construction also requires interpreting the term or phrase in light of other limitations in the claim, including the entire claim. *See Phillips*, 415 F.3d at 1314; *ACTV, Inc.*, 346 F.3d at 1082, *see also Hockerson-Halberstadt, Inc. v. Converse Inc.*, 183 F.3d 1369, 1374 (Fed. Cir. 1999) (finding that "[p]roper claim construction … demands interpretation of the entire claim in context, not a single element in isolation.").

[3] Relatedly, the prosecution history also distinguishes the claimed eye redness (hyperemia) from a red eye occurring due to subconjunctival hemorrhage. Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 7). These constitute vastly different ocular conditions. Trattler Decl. ¶ 52. Where hyperemia occurs when ocular blood vessels dilate, subconjunctival hemorrhage occurs when ocular blood vessels break open and blood pours out to settle beneath the conjunctiva, manifesting as large blood spot on the eye. Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 7); Trattler Decl. ¶ 52. A further important distinction is that once subconjunctival hemorrhage occurs, unlike ocular hyperemia, it cannot be reduced by vasoconstriction and will only dissipate with time. Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 7); Trattler Decl. ¶ 45.

The disputed claim phrase is part of the step of administering brimonidine to achieve the stated purpose of the claimed preamble "reducing eye redness in a human subject having ocular hyperemia." The preamble provides antecedent basis for the disputed phrase. It breathes life and meaning into the claim and is the raison d'etre for administering brimonidine as claimed to the human needing eye redness reduction. *Boehringer Ingelheim Vetmedica, Inc.v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003). Accordingly, reading the preamble together with the full claim element containing the disputed phrase, a POSA would have understood the disputed phrase to mean that the human subject of the claimed method has ocular hyperemia and the hyperemia is actually reduced by vasoconstriction. *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) (finding the preamble was a purposeful statement and, when read with the body of the claim directed to someone in need of that treatment, required the method be performed for that purpose); *Sanofi Mature IP v. Mylan Lab'ys Ltd.*, 757 F. App'x 988, 933 (Fed. Cir. 2019) (holding that claimed preamble of "[a] method of increasing survival" when read with claim language directed to a person in need thereof required increasing survival to practice the claimed method).

This plain claim language is consistent with the specification and prosecution history, which describe and clarify that the '600 patent methods require administering brimonidine as claimed to a human subject's hyperemic eyes to affirmatively reduce the hyperemia by vasoconstriction. The specification describes a key discovery of the invention as ***achieving*** significantly reduced hyperemia with more effective vasoconstriction. Ex. 1 ('600 patent), 2:51-55 ("One of the key discoveries of the present invention lies in using low doses of highly selective a-2 adrenergic receptor agonists to ***achieve*** vasoconstriction with significantly reduced hyperemia.") (emphasis added). Reducing eye redness in the conjunctiva, sclera and episclera

makes the eyes appear whiter. Trattler Decl. ¶ 36. The specification describes inventive methods of using brimonidine that achieve "a more effective scleral whitening … as a result of more effective vasoconstriction," Ex. 1 ('600 patent), 14:30-36, and discloses several clinical studies substantiating its claim in that regard, *e.g.*, Examples 1, 4, and 5 and the studies embodied in Figures 5A-C; *see Sanofi*, 757 F. App'x at 933 (finding the specification's emphasis on the importance of increasing survival supported construing claims to require "increasing survival").

The prosecution history similarly aligns with the claims and the specification. The Patentee introduced the disputed phrase by amending the claims "to recite that the human has ocular hyperemia, which is eye redness …, where such redness can be reduced by vasoconstriction of blood vessels." Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 7). Moreover, to distinguish Dean, the Patentee argued that "[t]he invention here demonstrates that low-dose brimonidine, used on a human subject having ocular hyperemia, affirmatively *reduces* eye redness…." *Id*. at 13 (emphasis in original). The Patentee repeatedly emphasized that the claimed method requires achieving redness reduction: "[N]or does [Dean] suggest using brimonidine, let alone low-dose brimonidine as the sole active ingredient, ***to affirmatively reduce eye redness in a patient having ocular hyperemia***." *Id*. (emphasis added). And Dean's teachings are "far from guiding the skilled artisan to about 0.025% as the sole active ingredient ***to affirmatively reduce redness in a person having ocular hyperemia***…." *Id*. (emphasis added). *See GPNE Corp. v. Apple Inc.*, 830 F.3d 1365, 1371 (Fed. Cir. 2016) (finding that the prosecution history which "consistently and exclusively" discloses the invention in a particular way supports a claim term construction that is consistent with the disclosure); *see also Wis. Alumni Rsch. Found. v. Apple Inc.*, 905 F.3d 1341, 1351 (Fed. Cir. 2018).

Thus, objectively reading the claims together with the specification and prosecution history, a POSA would have understood "human in need of said eye redness reduction" to mean "a human having ocular hyperemia, where such hyperemia is reduced by vasoconstriction."

2. Defendants' Proposed Construction Runs Directly Contrary to the Intrinsic Evidence

Defendants propose that "human in need of said reduction of eye redness" should be construed as "having ocular hyperemia." The Court should reject this construction. It renders the disputed phrase redundant to language in the preamble "in a human subject having ocular hyperemia" and thus adds nothing. *See Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so."); *see also VLSI Tech. LLC v. Intel Corp.*, 53 F. 4th 646, 655 (Fed. Cir. 2022) (noting that disputed phrase was added by amendment during prosecution and stating "[p]resumably, that phrase was meant to serve some purpose and should be construed to have some independent meaning" from separate phrase added in the same amendment). Contrary to Defendants' proposal, the disputed phrase is part of a manipulative step in the claimed method as a whole and must be given weight in that context. *See Rapoport v. Dement*, 254 F.3d 1053, 1058-61 (Fed. Cir. 2001) (construing a method of treating sleep apneas to a patient in need thereof to require administering the claimed compound to patients suffering from sleep apnea).

Defendants' construction moreover whitewashes the "in need of" language and eviscerates the disputed phrase's existence to ultimately foster Defendants' objective of advancing a reading of the claimed method as only an intent to reduce eye redness without any requirement for actually achieving redness reduction. Defendants interpreted the preamble in related U.S. Patent No. 8,293,742 ("the '742 patent")—a method of reducing eye redness—in a similar manner, presumably to lessen their burden of proving invalidity in view of the prior art because no results

would be required.[4] Defendants are wrong as a matter of law. *E.g.*, *Eli Lilly and Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331 (Fed. Cir. 2021) (requiring for obviousness evidence of reasonable expectation of successfully achieving the intended purpose of the limiting preamble even where motivation may exist). But even so, Defendants' proposed construction is inconsistent with the specification and prosecution history, which, as explained above, confirm that the '600 patent methods require administering brimonidine to a human subject's hyperemic eye(s) to affirmatively achieve reduction of the hyperemia by vasoconstriction.

For at least these reasons, Plaintiffs respectfully request that the Court adopt their proposed claim constructions for this disputed phrase and reject Defendants' litigation-driven construction.

B. The Court Should Adopt Plaintiffs' Proposed Construction of the Phrase "as the sole active ingredient"

1. Plaintiff's Proposed Meaning of "as the sole active ingredient" is Supported by the Claim Language and Confirmed by the Specification and Prosecution History

The parties also dispute the meaning of the phrase "as the sole active ingredient" recited in claim 1, which is incorporated in claims 12 and 28 by their dependency from claim 1. The Parties' respective proposed constructions for the phrase are shown below.

Plaintiffs' Construction	Defendants' Construction
"[administering brimonidine] as the only active ingredient to affirmatively reduce redness in a person having ocular hyperemia."	"without any other active ingredient in the ocular drop"

Reading "as the sole active ingredient" in context of the full '600 patent method and in view of the specification and prosecution history, a POSA would have understood it to mean

[4] Defendants filed an Inter Partes Review at the USPTO challenging the validity of the '742 patent, and in that proceeding, took the position that the claim preamble was limited only to as intent to reduce redness but did not require actual redness reduction. The USPTO's decision in that case is currently on appeal to the Federal Circuit.

"[administering brimonidine] as the only active ingredient to affirmatively reduce redness in a person having ocular hyperemia." Trattler Decl. ¶¶ 59-60. The prosecution history particularly evidences how the Patentee understood that phrase, having unequivocally surrendered and disclaimed the administration of brimonidine as part of a dosing protocol with any other active ingredient to distinguish the claimed methods from prior art. *Id*. at 61. Defendants propose that the phrase should be construed as "without any other active ingredient in the ocular drop." That proposal, however, opens the method to administering additional drops that contain other active ingredients, running directly contrary with how a POSA would have understood the phrase in light of the intrinsic record. *Id*. at 63.

Courts construe claims by starting with the claims themselves and interpreting them as a POSA would have in light of the specification and prosecution history. *See Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1276 (Fed. Cir. 2013) (relying primarily on intrinsic evidence like the claims themselves when construing claim terms); *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979-980 (Fed. Cir. 1995), aff'd, 517 U.S. 370, 116 S. Ct. 1384, 134 L. Ed. 2d 577 (1996) (explaining that claims are not interpretated in isolation but in view of the specification of which they are part and the patent's history of prosecution). The reference in the claims to brimonidine as the sole active ingredient would have been understood by a POSA as pertaining to the claimed method as a whole. Trattler Decl. ¶ 60. The ocular drop is merely the vehicle by which brimonidine, as the sole active agent in the claimed method, is administered. *Id*. In other words, whether one or multiple ocular drops are topically administered to reduce a person's ocular hyperemia, all administered medicated drops contain only brimonidine as the sole active ingredient. *Id*. That understanding aligns with both the specification and the prosecution

history, with the latter clearly dispelling any notion that the claimed method can read on administering any other active ingredient as part of the dosing protocol with brimonidine.

Indeed, the prosecution history can inform the meaning of claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in prosecution to distinguish over the prior art. *Kaken Pharm. Co., Ltd. v. Iancu*, 952 F.3d 1346, 1353 (Fed. Cir. 2020). Express representations made by the applicant to the Examiner to convince the Examiner of patentability and induce the patent grant can evidence and provide public notice of how the Patentee understood the claims, and can even make the claim scope different from what it would otherwise be. *Phillips*, 415 F.3d at 1317 (citing *Vitronics*, 90 F.3d at 1582–83); *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1095 (Fed. Cir. 2013) (construing claims consistent with the meaning ascribed to claim to obtain the patent); *SciMed Life Systems, Inc. v. Advanced Cardiovascular Systems, Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001) (finding disclaimer of a particular feature where the specification makes clear that the invention does not include that feature though the claims might otherwise be read broad enough to encompass that feature).

That is exactly what happened with the ’600 patent. During prosecution, the Patentee clearly and unmistakably surrendered and disclaimed the use of brimonidine with any other active agent and limited the claimed method to using brimonidine as the sole active ingredient to distinguish prior art (Dean) and induce the patent grant. *Kaken*, 952 F.3d. at 1353.

Specifically, to treat diseases like glaucoma and diabetic retinopathy, Dean taught combining brimonidine and brinzolamide in the same dosage protocol, either together or sequentially. Ex. 10 (Dean) at 2:55-57 (“When two separate formulations of brinzolamide and brimonidine are used, the preferred administration sequence is brimonidine first and brinzolamide

second."). In distinguishing Dean, the Patentee argued that "Dean is not directed to treating eye redness, nor does it suggest using brimonidine, ***let alone low-dose brimonidine as the sole active ingredient***, to affirmatively reduce eye redness in a patient having ocular hyperemia." Ex. 17 ('600 patent file history, November 4, 2022 Response to Office Action at 13) (emphasis added). "Rather, Dean is directed to ***combinations*** of brinzolamide and brimonidine for treating a different condition, i.e., lowering intraocular pressure (IOP)" (*id.*, emphasis original), and Dean, as argued by the Patentee, is "far from guiding the skilled artisan to about 0.025% ***brimonidine as the sole active ingredient*** to affirmatively reduce redness in a person having ocular hyperemia." *Id.* (emphasis added). "At bottom, [Dean] … does not teach or suggest that ***low dose brimonidine as the sole active*** can reduce redness…." *Id.* (emphasis added).

Where the patentee repeatedly and consistently characterized a claim phrase in a particular way, as here, it is proper to construe that phrase consistent with that characterization. *See GPNE Corp.*, 830 F.3d at 1371; *see also Wis. Alumni Rsch.*, 905 F.3d at 1351. The Patentee clearly and repeatedly disclaimed dosing brimonidine with any other active ingredient in the claimed methods, which are plainly directed to administering brimonidine as the sole active ingredient, in order to overcome the rejection based on Dean and procure allowed claims. *Kaken*, 952 F.3d. at 1353. Thus, the file history supports construing the phrase "as the sole active ingredient" as a requirement of the claimed methods, such that, whether one or multiple medicated drops are dosed as part of the methods to reduce eye redness, brimonidine is the only active ingredient in all of those drops. Trattler Decl. ¶ 60.

The interpretation finds support in specification. The specification discloses various inventive embodiments, some of which dose brimonidine in combination with other active ingredients, *see*, *e.g.*, Ex. 1 ('600 patent), 9:53-55, 15:61-17:3, 16:57-58, 65-66, and others that

dose brimonidine as the sole active ingredient. *See, e.g.*, *id*. at 7:34-40, 8:19-25, 9:46-49, 10:21-26, Examples 1, 4, and 5 and the studies embodied in Figures 5A-C. A POSA reading the '600 patent claims in view of the specification would have understood that the patentee was claiming the embodiment of dosing brimonidine as the sole active ingredient to reduce the person's ocular hyperemia. Trattler Decl. ¶ 62.

2. Defendants' Proposed Construction Would Improperly Reclaim Subject Matter Disclaimed During Prosecution

In interpreting "as the sole active ingredient," Defendants propose that it applies only to the "ocular drop," thereby rendering the claim open to separate drops that can contain other active ingredients. Such an interpretation, however, would improperly recapture what the patentee disclaimed during prosecution to distinguish Dean, which specifically disclosed sequential administration of separate formulations of brimonidine in one formulation and brinzolamide in the other. *See Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1573 (Fed. Cir. 1997) (finding that surrendered subject matter from a prosecution history disclaimer cannot be re-asserted); *see also Traxcell Techs., LLC v. Nokia Sols. & Networks Oy*, 15 F.4th 1136, 1146 (Fed. Cir. 2021) (finding that patent scope which was clearly and unmistakably surrendered during prosecution to be "lost territory" which cannot be reclaimed). Properly interpreted, therefore, the prosecution history dispels any notion that the claimed method can read on administering any other active ingredient as part of the dosing protocol with brimonidine, whether in one or multiple ocular drops.

For these reasons, Plaintiffs respectfully request that the Court reject Defendants' construction adopt Plaintiffs proposed claim constructions for this disputed phrase.

VI. CONCLUSION

For at least the foregoing reasons discussed above, Plaintiffs respectfully request that this Court adopt Plaintiffs' proposed claim constructions and reject Defendants' constructions.

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Respectfully submitted,

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